ICH Q12: A Much Needed Culture Shift

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Outline

• Q12 background
• Proposed content
• Enablers
• Lifecycle discussion
Q12 Background

• Proposed by the Informal Quality Discussion Group (IQDG) and accepted by the ICH Steering Committee in Minneapolis, June 2014

• Perceived problems to be addressed:
  – Lack of alignment regarding necessary information and level of detail in the application
  – Desire for more post-approval ‘operational flexibility’ regarding change management
  – Realize intended benefits that result from Q8, Q9, Q10, Q11 implementation
  – Reduce perceived regulatory barriers to continual improvement
Goals for ICH Q12

- Clarify necessary information and level of detail for application
- Harmonize approaches for technical and regulatory aspects of lifecycle management
- Create opportunities to prospectively manage future changes in a more strategic manner
- Facilitate post approval changes and continual improvement
- Develop ICH focus for ‘post launch’ stages of the lifecycle
Desired State

• “A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high-quality drug products without extensive regulatory oversight”

• Most manufacturing changes are managed effectively under the company’s Pharmaceutical Quality System (PQS) without the need for regulatory approval prior to implementation
Proposed Q12 Content

- Guiding Principles
- Established Conditions
- Post Approval Change Management Protocols
- Lifecycle Management Strategy
- Pharmaceutical Quality System and Change Management
- Application of Q12 to currently marketed products
- Examples
Established Conditions (EC)

• Working Definition:

  Binding information defined in an application. A change to an established condition (e.g., beyond specified range, unit step description… ) as defined in an approved application would initiate a post-approval regulatory submission.

  Note: Information that is not an EC would not need to be reported if changed (but would still need to be managed under the PQS)

• EC proposals should be science and risk based (Q8,Q9,Q11)

• Brings clarity to the link between patient needs and product quality attributes, processes, and material attributes
Postapproval Change Management Protocols

- Also known as “Comparability Protocols”
- Regulatory tool for post-approval changes
  - Outline specific future change(s) to be made
  - Tests, studies, etc. to be conducted to verify acceptability of change
  - Propose reporting category; often reduced compared to existing guidance
- FDA draft guidance “Comparability Protocols for Human Drugs and Biologics” – April 2016
- EU introduced Post-approval change management protocols (PACMPs) in 2010
- Similar concepts in both FDA and EU approaches
Product Specific Lifecycle Strategy

• Document that summarizes:
  – ECs and justification
  – EC management
  – Commitments
  – Reporting categories
  – PACMPs
  – Plans for major changes during the product lifecycle (if known) to enable continuous improvement

Note: Does not speak for the totality of product lifecycle management

• Provides a central platform that supports knowledge management and transparency over the lifecycle, between and within industry and regulator
PQS

- ICH Q12 will build on ICH Q10
- Focus on the “effective PQS”
- Elaboration on the CM process highlighting essentiality of KM and QRM
- Linkage between sponsor and sites PQS’s
  - stewards of quality oversight and knowledge
- Use of active knowledge management to drive change over the lifecycle
  - Harness sources of knowledge to identify areas of improvement and optimization
Key Enablers

• Q12 essentially relies on:
  – Robust product process understanding
    • ICH Q8, Q9, Q11
  – Effective PQS
    • ICH Q10
Key Enabler 1

• Robust product and process understanding
  – Clear understanding of the product, manufacturing process, facilities and equipment, and elements of the associated control strategy that assure process performance and product quality
  – Drives the company and the regulator towards clear justification for established conditions
  – Influences scope of regulatory PAC flexibility
  – Provides context for lifecycle strategy elements
Key Enabler 2

• An ‘effective’ PQS
  – Integrates Q10 elements across disciplines over the lifecycle
  – Employs active knowledge and quality risk management
  – Engages robust quality vigilance in leading to effective change management
    • Utilize data from the appropriate sources with patient-centric, risk-based principles
  – Drives company toward quality culture
  – Provides confidence that most changes can be managed solely under the company’s PQS
    • May influence PAC reporting categories
  – Provides confidence in the context of key enabler 1
ECs and Change Management

Overall control strategy including facility, environmental controls, etc. (Not typically reported in submission)

Supportive of product, process, controls, etc.

Changes reportable Post-approval
ICH Q12: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management

For Q12 to achieve its full potential, we have to be willing to change the way we think about and the way we interact over the lifecycle
About The Original Application

• No longer the end goal
  − The investment in energy and resources can’t solely be about the original application approval
• Rather, we could be thinking about it as a milestone during the lifecycle.
• A snapshot that provides:
  − Clarity on development leading to the proposed product/process/control strategy
  − Proposed ECs and justification
  − Launching pad for EC and change management
  − Plans for future changes, if known
About Development

- Has to go beyond the proposed product, process, control strategy, etc… for the original application
- It has to continue beyond approval
  - Prospective monitoring and verification of initial assumptions / conclusions
  - Maintain the ability to learn and improve
- The desire to keep improving will drive the behavioral change that Q12 requests
About The Interaction Between Sponsor and Sites

• Sites should be seen as source of knowledge, not just ‘producers’
• Recognize the difference and necessary partnership between EC owners and data / knowledge creators
• All sites play a role in confirmation and continual improvement
• Realize the benefit of integrating this knowledge for EC management
“Effective” PQS
Integrated / Effective PQS
About the Lifecycle

• ECs could be determined due to known risk, uncertainty, or both
• Need to consider how to holistically manage risk, uncertainty, and ECs during post approval stages in lifecycle
• Intentional prospective thinking, transparent communication, and accountability could support:
  – An integrated organizational approach throughout the lifecycle
  – Flexibility with EC PAC reporting
About the Lifecycle

• Can’t think of these as separate elements
About the Lifecycle

• Have to put these elements together to see the bigger picture of product lifecycle management
Benefits

• Incentivize implementation of Q8-Q11
• Incentivize, enable, and encourage increased transparency:
  − Within a company
  − Between sponsor and CMOs
  − Between industry and regulatory agency
  − Within the regulatory agency
• Confidence in how the firm will manage itself
Benefits

• Reduce unnecessary cost and time burdens on both industry and regulators
• Assure that patients have reliable access to high quality therapies
• Products benefit from application of current and innovative manufacturing technologies
• Clarity for post approval reporting: right changes, right notification level
Changing Culture

- Enhanced transparency and trust between company and regulator
- Focus time and effort on higher risk issues
- Shift more post approval lifecycle management back to the industry
- Achieve the ‘21st century’ desired state
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